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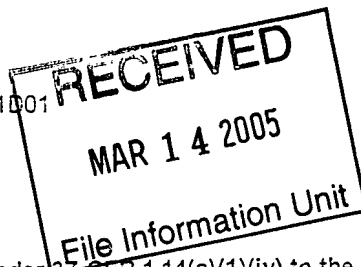
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In re Application of

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08/147,912

11/3/93

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I hereby request access under 37 CFR 1.14(a)(1)(iv) to the application file record of the above-identified ABANDONED application, which is identified in, or to which a benefit is claimed, in the following document (as shown in the attachment):

United States Patent Application Publication No. 5,677,177 page, _____ line _____.

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US005677177A

United States Patent [19]

Wahl et al.

[11] **Patent Number:** 5,677,177[45] **Date of Patent:** Oct. 14, 1997

[54] **FLP-MEDIATED GENE MODIFICATION IN MAMMALIAN CELLS, AND COMPOSITIONS AND CELLS USEFUL THEREFOR**

4,997,757 3/1991 Schiestl 435/172.1

[75] **Inventors:** Geoffrey M. Wahl; Stephen V. O'Gorman, both of San Diego, Calif.

[73] **Assignee:** The Salk Institute for Biological Studies, La Jolla, Calif.

[21] **Appl. No.:** 486,409

[22] **Filed:** Jun. 7, 1995

Related U.S. Application Data

[62] Division of Ser. No. ~~147,912~~, Nov. 3, 1993, which is a continuation of Ser. No. 666,252, Mar. 8, 1991, abandoned.

[51] **Int. Cl.⁶** C12N 5/06; C12N 15/09; C12N 15/90

[52] **U.S. Cl.** 435/325; 435/172.3; 435/320.1; 435/350; 435/351; 435/352; 435/353; 435/354; 435/363; 435/366; 435/193; 435/197; 435/194; 536/24.2; 536/24.1; 536/23.74; 536/23.1; 935/66; 935/8; 935/22; 514/44; 800/2

[58] **Field of Search** 800/2; 435/172.1, 435/172.2, 172.3, 240.2, 240.21, 320.1, 350, 351, 352, 353, 354, 363, 193, 197, 194; 514/44; 536/23.1, 23.74, 24.1, 24.2; 935/52, 55, 56, 57, 58, 69, 70, 71, 72, 22, 8

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[57] **ABSTRACT**

A gene activation/inactivation and site-specific integration system has been developed for mammalian cells. The invention system is based on the recombination of transfected sequences by FLP, a recombinase derived from *Saccharomyces*. In several cell lines, FLP has been shown to rapidly and precisely recombine copies of its specific target sequence. For example, a chromosomally integrated, silent β -galactosidase reporter gene was activated for expression by FLP-mediated removal of intervening sequences to generate clones of marked cells. Alternatively, the reverse reaction can be used to target transfected DNA to specific chromosomal sites. These results demonstrate that FLP can be used, for example, to mosaically activate or inactivate transgenes for a variety of therapeutic purposes, as well as for analysis of vertebrate development.

24 Claims, 3 Drawing Sheets